The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

# UNITED STATES PATENT AND TRADEMARK OFFICE

# BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte SIMON C. BURTON, DAVID R.K. HARDING, NATHANIEL T. BECKER, BEN A. BULTHUIS, and LANDON M. STEELE

Appeal No. 2005-1344[1]
Application No. 08/468,610

MAILED

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U.S. PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS
AND INTERFERENCES

HEARD: November 15, 2005

Before ELLIS, SCHEINER, and ADAMS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

VACATUR and REMAND TO THE EXAMINER

On consideration of the record, we find this case is not in condition for a decision on appeal. We recognize that the application on appeal has been pending for more than nine years. However, for the following reasons, and as admitted by appellants' representative during the November 15, 2005 Oral Hearing, the examiner and appellants have not had a "meeting of the minds" on how to interpret the claimed invention. We remind the examiner and appellants that analyzing claims based on "speculation as to meaning of the terms employed and assumptions as to the scope of such claims" is legal error. In re

[1] This application is a divisional of Application No. 08/268,178, filed June 29, 1994. The subject matter on appeal is related to copending Appeal No. 2005-1443 (Application No. 08/654,937), which is a continuation of Application No. 08/268,178. Accordingly, we have considered Appeal Nos. 2005-1443 and 2005-1344 together.

Steele, 305 F.2d 859, 862, 134 USPQ 292, 295 (CCPA 1962). Accordingly, we vacate[2] the rejections of record and remand the application to the examiner to consider the following issues and to take appropriate action.

Claims 1-5, 7-23, 55 and 56 are before us on appeal. Claims 6, and 24-54 have been cancelled[3].

Claims 1 and 16 are illustrative of the subject matter on appeal and are reproduced below:

1. A resin-protein/peptide complex which comprises a resin and a target protein or peptide bound thereto wherein said resin comprises
   a) a solid support matrix; and
   b) selected ionizable ligand covalently attached to the matrix wherein the ionizable ligand is selected such that the resin is electrostatically uncharged at a high and a low ionic strength at the pH where the target protein or peptide is bound to the resin wherein the protein or peptide binds to the resin at a pH of 5 to 9 and is electrostatically charged at the pH where the target protein or peptide is desorbed from the resin wherein desorption occurs by a change in the pH from the binding pH and further wherein about 50 percent or more of the target protein or peptide in an aqueous medium binds to the resin when the aqueous medium has either a high or a low ionic strength.

16. A resin-protein/peptide complex which comprises a resin and a target protein or peptide bound thereto wherein said resin comprises
   a) a solid support matrix having a selected ionizable functionality incorporated into the backbone thereof wherein the ionizable functionality is selected such that the resin is electrostatically uncharged at a high and a low ionic strength at the pH where the target protein or peptide is bound to the resin wherein the protein or peptide binds to the resin at a pH of 5 to 9 and is electrostatically charged at the pH where the target protein or peptide is desorbed from the resin wherein desorption occurs by a change in the pH from the binding pH; and
   b) optionally a non-ionizable ligand covalently attached thereto, wherein about 50 percent or more of the target protein or peptide in

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[2] Lest there be any misunderstanding, the term "vacate" in this context means to set aside or to void. When the Board vacates an examiner's rejection, the rejection is set aside and no longer exists.

[3] See Paper received June 6, 1995, page 2, paragraph 7.

an aqueous medium binds to the resin when the aqueous medium has either a high or a low ionic strength.

The references relied upon by the examiner are:

| | | |
|---|---|---|
| Economy et al. (Economy) | 3,835,072 | Sep. 10, 1974 |
| Jones et al. (Jones) | 4,154,676 | May 15, 1979 |
| Hancock et al. (Hancock) | 4,401,629 | Aug. 30, 1983 |
| Bruegger | 4,810,391 | Mar. 7, 1989 |
| Iimuro et al. (Iimuro) | 4,950,807 | Aug. 21, 1990 |
| Tokuyama (PTO 04-4920 translation relied upon) | JP 60-137441 | Jul. 22, 1985 |
| Kondo et al. (Kondo) (PTO 04-4918 translation relied upon) | JP 61-033130 | Feb. 17, 1986 |
| Kitamura et al. (Kitamura) (PTO 04-4919 translation relied upon) | JP 01-211543 | Aug. 24, 1989 |

Topp et al., (Topp), "Properties of Ion-Exchange Resins in Relation to their Structure. Part 1. Titration Curves," J. Chem. Soc., pp. 3299-3303 (1949)

Boardman et al., (Boardman) "Separation of Neutral Proteins on Ion-Exchange Resins," Nature, Vol. 171, pp. 208-210 (1953)

Kitchener, "Properties and Behavior, 5. Effect of pH on Exchange Equilibria" in Ion Exchangers in Organic and Biochemistry, pp. 63-65 (Calvin Calmon et al., eds., Interscience Publishers, Inc., New York, 1957)

Guthrie, "Ion Exchangers of Plant Origin, and Use of Resins in Plant Chemistry" in Ion Exchangers in Organic and Biochemistry, pp. 558-559 (Calvin Calmon et al., eds., Interscience Publishers, Inc., New York, 1957)

(Kunin), "Cation Exchange Resin Characteristics" in Ion Exchange Resins, pp. 34-39 (Robert Kunin ed., John Wiley & Sons, Inc., New York, 1958)

Sasaki et al. (Sasaki I) "Hydrophobic-Ionic Chromatography, Its Application to Purification of Porcine Pancreas Enzymes," J. Biochem., Vol. 86, pp. 1537-1548 (1979)

Sasaki et al. (Sasaki II) "Hydrophobic-Ionic Chromatography, Its Application to Microbial Glucose Oxidase, Hyaluronidase, Cholesterol Oxidase, and Cholesterol Esterase," J. Biochem., Vol. 91, pp. 1555-1561 (1982)

## GROUNDS OF REJECTION

Claims 1, 2, 4, 5, 10-16, 18, 20, 22 and 23 stand rejected under 35 U.S.C. § 102(b) as anticipated by Boardman.

Claims 1-5, 7-23, 55 and 56 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on the combination of Boardman, Sasaki I, Sasaki II, Kunin, Topp, Kitchener, Guthrie, Hancock, Kitamura, Tokuyama, Kondo, Iimuro, Bruegger, Economy and Jones.

We vacate the rejections of record and remand the application to the examiner for further consideration.

## DISCUSSION

Claim Construction:

While there are four independent claims pending in this appeal, we believe claims 1 and 16 to be representative of the issues that need to be resolved before taking any further action on the merits of this application. Accordingly, we limit our analysis to independent claims 1 and 16.

As we understand it, claim 1 is drawn to a resin-protein/peptide complex which comprises a resin and a target protein or peptide bound thereto. The claim requires the resin to comprise (a) a solid support matrix; and (b) a selected ionizable ligand covalently attached to the matrix. In addition the claim requires:

i) the ionizable ligand to be selected such that the resin is electrostatically uncharged at a high and a low ionic strength at the pH where the target protein or peptide is bound to the resin,

ii) the protein or peptide to bind the resin at a pH of 5 to 9,

iii) the protein or peptide to be electrostatically charged at the pH where the target protein or peptide is desorbed from the resin,

iv) desorption to occur by a change in the pH from the binding pH, and

v) about 50 percent or more of the target protein or peptide in an aqueous medium binds to the resin when the aqueous medium has either a high or a low ionic strength.

As discussed below, and emphasized by the underlining above, the intent of a number of phrases and terms in appellants' claims is unclear.

Ionizable ligand covalently attached to the matrix

According to appellants' specification (page 15), "[t]he term 'ionizable ligand' refers to a group covalently attached to the solid support matrix either directly or through a spacer arm which group contains one or more functionalities capable of being electrostatically charged at one pH and electrostatically uncharged at another pH." Appellants list a number of "[s]uitable ionizable ligands," which include carboxyl groups. See Id. As we understand it, appellants' Figures 8A through 8C illustrate an ionizable group covalently attached to the solid support matrix either directly (Figures 8A[4] and 8C[5]) or through a spacer arm (Figure 8B[6]).

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[4] "Figure 8A illustrates direct covalent attachment of the ligand to the solid support matrix...." Specification, page 16.

[5] "Figure 8C illustrates a resin having ionizable functionality or a mixture of ionizable functionalities incorporated into the backbone of the solid support matrix." Specification, page 17.

[6] "Figure 8B illustrates covalent attachment of the ligand to the solid support matrix via a suitable spacer arm incorporated into and comprising part of the ligand...." Specification, page 17.

While appellants disclose (specification, page 17) that "Figure 8C illustrates a resin having [an] ionizable functionality or a mixture of ionizable functionalities incorporated into the backbone of the solid support matrix," we find no evidence of record to suggest that these functionalities are not "incorporated" through covalent bonds. Nevertheless, in addressing the anticipation rejection, appellants assert (Brief, page 8) that the "ionizable functionality on the [Amberlite IRC 50®] resin [taught by the Boardman prior art reference] is a carboxylic acid group, which in incorporated into the resin when it is synthesized." According to appellants (id.), "the ionizable group of IRC-50 is part of the resin's solid support matrix; it is not covalently attached to the matrix through a chemical transformation." We must admit that this assertion is somewhat puzzling – if not through a covalent bond, how is the ionizable group on the Amberlite IRC 50® resin "incorporated" into the resin when it is synthesized? Appellants fail to favor this record with any evidence demonstrating that the ionizable group on the Amberlite IRC 50® resin, or on a resin such as the one illustrated in appellants' Figure 8C, is not covalently attached. The examiner also fails to develop this record by routing out the proper construction of the claimed invention. Instead, the examiner simply asserts (Answer, page 16), "[a]ppellant's [sic] claims simply do not exclude resins having the ionizable ligand as part of the solid matrix."

Upon consideration of the record, we find that appellants disclose (specification, bridging paragraph, pages 17-18),

> [t]he phrase "a solid support matrix having a selected ionizable functionality incorporated into the backbone thereof" as

> employed herein refers to a solid support matrix containing within its backbone an ionizable functionality. Such ionizable functionalities are similar to ionizable ligands with the exception that the ionizable ligand is pendent to the backbone of the solid support matrix whereas the ionizable functionality is incorporated into the backbone.

On reflection, it may be that appellants' intended the term "ionizable groups" in their statements regarding the Amberlite IRC 50® resin to mean "ionizable functionalities," which are part of the backbone of the solid support matrix, and therefore differ from "ionizable ligands," which are pendent to the backbone of the solid support matrix.

For clarity, we direct attention to claims 1 and 16. Claim 16 refers to "a solid support matrix having a selected ionizable functionality incorporated into the backbone thereof" instead of an "ionizable ligand covalently attached to the matrix" as set forth in claim 1. While the Brief, and Answer fail to make it clear, it appears that this difference in terminology is significant. Specifically, claim 16 requires the selected ionizable functionality to be incorporated into the backbone of the matrix.[7] Stated differently, while claim 1 appears to be directed to a resin of the type illustrated in Figure 8A of appellants' specification, claim 16 appears to be directed to a resin of the type illustrated in Figure 8C of appellants' specification.

The record before us on appeal, however, does not clearly address this construction of the claimed invention. Specifically, as discussed above, the examiner fails to appreciate this difference in the claims.

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[7] See Brief, page 10, wherein appellants assert, "[i]ndependent claim 16 is similar to claim 1 discussed above, with at least one exception: the resin's ionizable functionality is incorporated into the backbone of the solid support matrix."

pH 5-9 and electrostatic charge

During the November 15, 2005 Oral Hearing, appellants' representative was questioned a number of times as to the intended meaning of the phrase pH 5-9 as it is used in the context of the claimed invention. According to appellants' representative, the phrase "pH of 5 to 9" refers to a pH range wherein throughout the entire pH range from 5 through 9, the target protein/peptide is bound and remains bound to the resin. This statement appears to be consistent with appellants' summary of the claimed invention, wherein appellants state (Brief, page 3),

> [r]esins of the present invention are selected such that the ionizable ligand is uncharged at a pH where the target protein or peptide is bound to the resin and electrostatically charged[8] at a pH where the target protein or peptide is desorbed from the resin. ... Resins of the present invention ... are uncharged in a pH range of 5-9. See p. 29, lns 24-28.

The examiner appears to agree with this interpretation of the claimed invention. See Answer, page 5, "[a] complex ... is claimed wherein the complex is formed at a pH value of between 5-9, where the resin is uncharged, and the target protein is bound to the resin by hydrophobic interactions."

This construction of the claimed invention, however, does not appear to be supported by appellants' specification. At page 29, lines 24-28, appellants' specification discloses "the ionizable ligands attached to the solid support matrix should provide resins which begin to titrate (become electrostatically charged) in a pH range of from about 5 to 9 and more preferably from about 5.5 to about

[8] According to appellants' specification (page 18), the term "electrostatically uncharged" "means that less than 5% of the ionizable functionalities on the resin are charged at the pH of target protein binding."

8.5." Thus, contrary to appellants' assertion (Brief, page 3), according to appellants' specification (page 29, lines 24-28), resins of the present invention become electrostatically charged in a pH range of from about 5 to 9.

In addition, despite the examiner's construction of the complex set forth in appellants' claimed invention (Answer, page 3), wherein the resin is electrostatically uncharged at a pH from 5 to 9, the examiner's anticipation rejection goes counter to this construction of the claimed invention. Specifically, as we understand it, the examiner applies Boardman as an anticipatory reference because it teaches a target protein tightly bound to an electrostatically uncharged resin at pH 5, and desorbed from an electrostatically charged resin at pH 6-7. See Answer, page 5.

On reflection, we are left with a construction of the claimed invention by the examiner and appellants that appears to be contrary to both appellants' specification and the examiner's application of prior art.

### 50 percent or more

According to appellants' claimed invention (see e.g., claim 1), "50 percent or more of the target protein or peptide in an aqueous medium binds to the resin when the aqueous medium has either a high or a low ionic strength." As we understand it, the claims are drawn to a resin-protein/peptide complex. Accordingly, the intent of the last clause of, for example, claim 1, is less than clear. As it now stands, it is our opinion that the clause is open to at least two different interpretations. First, that 50 percent or more of the target protein or

peptide on the resin-protein/peptide complex remains bound to the resin when in an aqueous medium of either a high or low ionic strength. Second, that 50 percent or more of the target protein or peptide in an aqueous media will bind the resin-protein/peptide complex.

We encourage appellants and the examiner to work together to clarify this issue.

## Conclusion

As the record stands before us on appeal, there is no discussion of the differences in the scope of the claims. Further, to the extent that some claim terms are construed on this record, the art is applied in a manner that appears to be contrary to the construction of the claim. Accordingly, we find this record is not in condition for a decision on appeal. As set forth in In re Zletz, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989):

> [D]uring patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed. . . . An essential purpose of patent examination is to fashion claims that are precise, clear, correct, and unambiguous. Only in this way can uncertainties of claim scope be removed, as much as possible, during the administrative process.

For the foregoing reasons, we vacate the rejections of record and remand the application to the examiner. Prior to taking any further action on the merits of this application, we encourage the examiner to take a step back and reconsider the scope of each claim, together with the specification and available prior art. The examiner should then clearly record a construction of the claims. The examiner should clearly identify any ambiguities in the meaning of claim terms

and take appropriate action. In the event that the examiner believes that a prior art rejection should be made, the examiner should clearly articulate the prior art rejection, insuring that all limitations of the rejected claims are accounted for.

In addition, we note that appellants should not be bystanders to the development of the administrative record. To the contrary, we encourage appellants to work together with the examiner to insure that their claims accurately reflect their invention. In this regard, we encourage appellants to take a step back and review their specification to insure that claims accurately reflect their invention. In the event that they do not, we encourage appellants to take appropriate action. Thereafter, we encourage appellants to work together with the examiner to properly develop the record of this application.

## OTHER ISSUES

While we take no action on the merits of this appeal, we make the following observations in an effort to advance the prosecution of this application.

I. The Brief appears to be inaccurate:

a. Ionic strength:

During the November 15, 2005 Oral Hearing, appellants' representative was questioned a number of times as to the intended meaning of the phrase "a high or a low ionic strength" as it is used in the context of the claimed invention. See e.g., last line of claim 1. According to appellants' representative, the phrase should be construed to read "a high and low ionic strength." See Brief, page 6,

> the claim recites that the resin is electrostatically uncharged at the pH where the target protein or peptide is resin bound, regardless of whether the medium is at a high or a low ionic strength. In other words, less than 5% of the resin's ionizable functional groups are ionized at a high ionic strength at a binding pH; and, less than 5% of the resin's ionizable functional groups are ionized at a low ionic strength at a binding pH.

The examiner finds, however, "the specification at page 18 defines 'high' ionic strength as greater than 250 millimolar. However, that limitation does not appear in the claims under examination. On the current record the term 'high' can be construed to encompass any concentration which is higher than another."

In our opinion, neither the appellants' nor the examiner appear to have interpreted this limitation correctly. According to appellants' specification (page 5), "[t]he resins described herein are further characterized as being capable of binding the target protein or peptide from a solution maintained at either high or low ionic strength." At page 18 of their specification appellants define the terms "high ionic strength" and "low ionic strength" as follows:

> The term "high ionic strength" means an ionic strength greater than or equal to that required to provide a conductivity of 4.7 millimho (milliSeimens ($mS/cm^2$)). For example, such conductivity can be reached by using 250 millimolar (mM) sodium chloride. The term "low ionic strength" means an ionic strength less than 4.7 millimho.

We understand from page 18 of appellants' specification in their related application (Application No. 08/654,937, Appeal No. 2005-1443), as amended by the Paper received July 20, 1995,[9] that a conductivity of 4.7 millimho corresponds to a 42 millimolar sodium chloride solution. Accordingly, we understand the term "high ionic strength" to mean an ionic strength equal to, or

[9] We note that a similar amendment to page 18 of the specification was not made in this application.

greater than a 42 mM sodium chloride solution, while the term "low ionic strength" means an ionic strength less than a 42 mM sodium chloride solution. Taken together, as appellants assert the limitation should be read, the limitation reads on any ionic strength. In our opinion, if the limitation is read according to appellants' assertion, the references to "high" and "low" as the terms appear in appellants' claims become meaningless. When read in the alternative, however, a high ionic strength would be anything equal to, or greater than a 42 mM sodium chloride solution, while a low ionic strength would be anything below a 42 mM sodium chloride solution. Stated differently, unlike appellants' construction of the phrase, the terms "high" and "low" appear to be meaningful only when read in the alternative. In addition, unlike the examiner's construction of the term, a high ionic strength is any ion concentration that provides a conductivity greater than or equal to 4.7 millimho.

Further, we direct attention to appellants' apparent misunderstanding of their disclosure. According to appellants (Brief, page 8), "[a]pplicants, ... define 'high ionic strength' to be a sodium ion concentration of about 250 mM or above." This is incorrect. According to appellants' specification (page 18), a "high ionic strength" "means an ionic strength greater than or equal to that required to provide a conductivity of 4.7 millimho (milliSeimens ($mS/cm^2$))." While a sodium ion concentration of about 250 mM would be an example of such an ion concentration, as we understand it from appellants' co-pending application, a conductivity of 4.7 millimho corresponds to a 42 millimolar (mM) sodium chloride solution. Thus any sodium chloride concentration of 42 mM or

above would be included in appellants' definition of high ionic strength. We encourage appellants to clarify this issue.

b. Polarity:

Claim 15 depends from and further limits claim 1 to require that the electrostatic charge induced on the resin of the resin-protein/peptide complex is of the opposite polarity from the net electrostatic charge on the target protein or peptide at the pH of desorption. According to appellants (Brief, page 9), Boardman teaches that cytochrome c is desorbed from the resin at a pH where both Amberlite IRC 50® and cytochrome c have net negative charges. As we understand it, this statement is incorrect. We believe it to be a well known biochemical principal that at a pH below its pI a protein will carry a net positive charge, and at a pH above its pI a protein will carry a net negative charge. Boardman teaches that the pI of cytochrome c is 10.1. Boardman, page 209, first column, third full paragraph. According to Boardman "[c]ytochrome c (isoelectric point 10.1) is desorbed ... as the pH rises from 8 to 10, but is not desorbed under acidic conditions." Id. A pH from 8-10, is below the pI of cytochrome c, accordingly it appears that while the Amberlite IRC 50® will exhibit a net negative charge at this pH, cytochrome c will have a net positive charge. Thus, the desorbing solution taught by Boardman for use in eluting cytochrome c has a pH which induces an electrostatic charge on the resin wherein the induced charge is of the opposite polarity as the net charge on the target protein or peptide at the pH of the desorbing solution. Thus, it would appear that the electrostatic charge induced on the resin of the resin-cytochrome c complex is of

the opposite polarity from the net electrostatic charge on the target protein or peptide at the pH of the desorption.

In the context of haemoglobins the opposite is true. Boardman refers to the illustration in Figure 1a and states (page 210, column 1, first full paragraph),

> as is show in Fig. 1a, at pH 5 the carboxylic groups of the resin are almost wholly undissociated, and adsorption of the haemoglobins is complete and irreversible. The elution volume – pH data of the haemoglobins may thus be represented by a family of steep curves falling rapidly from very high values to zero in the narrow range pH 5-6, the curves for the more acidic proteins being displaced to the left of those for proteins with higher isoelectric points."

To clarify, according to Boardman (page 210, column 1, first full paragraph), in the citrate buffer used for the chromatographic experiments, the isoelectric point of bovine and sheep foetal carboxyhaemoglobin lies between 4 and 5. Since a protein will carry a net negative charge at a pH above its pI, at a pH of 6, which is above the pI for bovine and sheep foetal carboxyhaemoglobin, each of the carboxyhaemoglobin proteins will have a net negative charge. See, Boardman, page 210, column 1, first full paragraph.

We encourage appellants to clarify this issue.

II. Becker Declaration:

We recognize appellants' arguments relating to the Becker declaration and the "Rohm and Haas product literature" discussed therein. Brief, pages 7-8. However, upon review of the Becker declaration, we note that declarant states that the Amberlite IRC 50® resin used by Broadman "becomes fully protonated (neutralized)[, completely uncharged,] only at a pH of between 2.5 and 4.0,

depending on the buffer salts present, and that the resin "remains charged at the pH where it binds the protein." Becker declaration, paragraph 9. We note, however, that declarant makes no attempt to clarify whether "less than 5% of the ionizable functionalities on the resin are charged at the pH of target protein binding," which is the definition set forth in appellants' specification for the term "electrostatically uncharged". See e.g., specification, page 18. Further, while declarant recognizes that resin properties will change depending on the buffer system that is used (see Declaration, paragraph 9), declarant makes no attempt to address the effect that Boardman's buffer may have on the Amberlite IRC 50® resin.

Upon review of the "Rohm and Haas product literature", specifically figure 3, it appears that at a pH of 5.0, the resin is "electrostatically uncharged", as defined at page 18 of appellants' specification, in all three of the titration curves set forth in figure 3. Thus, while we agree with declarant that the Amberlite IRC 50® resin is electrostatically charged at a pH where it binds the protein, e.g., pH 5.0, there is no evidence on this record to dispute that the charge on the resin is not within the scope of appellants' claimed invention.

Further, we note the examiner's recognition that the Amberlite IRC 50® resin has a "capacity of 10 Meq/g." Nevertheless, the examiner points out (Answer, bridging paragraph, pages 14-15), Figure 1a of Boardman, demonstrates that "[a]t pH 5.0, at the lower sodium concentration ... (curve 'B'), the resin takes up about 0.4 mg-equivalent sodum ions/gm of dry resin." According to the examiner (id.), this means that less than 5% of the ionizable

functionalities (the carboxyl groups) on the resin are charged at a pH of 5.0, the pH of target protein binding. The examiner appears to reach this conclusion by dividing the amount of sodium ions adsorbed by the resin at a pH of 5.0 (approximately 0.4 mg-equivalent sodium ions/gm of dry resin) by the total amount of sodium ions that can be adsorbed by the resin (approximately 8.8 mg-equivalent sodium ions/gm of dry resin) and then multiplying the result by 100%. Id. The examiner's calculation, however, does not appear to take into consideration the total capacity of the resin – 10Meq/g, or the effect, if any, that Boardman's buffer may have on the resin's capacity.

We encourage the examiner to clarify this issue.

III. Obviousness:

Prima facie obviousness based on a combination of references requires that the prior art provide "a reason, suggestion, or motivation to lead an inventor to combine those references." Pro-Mold and Tool Co. v. Great Lakes Plastics Inc., 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996).

> [E]vidence of a suggestion, teaching, or motivation to combine may flow from the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved.... The range of sources available, however, does not diminish the requirement for actual evidence. That is, the showing must be clear and particular.

In re Dembiczak, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) (citations omitted). The suggestion to combine prior art references must come from the cited references, not from the application's disclosure. See In re Dow Chemical Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

On the record presented for our review, we note that the obviousness rejection presented a number of references directed to various chromatography resins. While we would not dispute that these chromatography resins exist, we question why a person of ordinary skill in the art would apply such resins against appellants' claimed invention. For example, we note that Hancock, as relied upon by the examiner, states (column 1, lines 10-14), "the invention is concerned with the provision of ion exchange resins capable of being utilized to separate copper, nickel and cobalt both from each other and also from other metals in solution." Appellants' claimed invention is concerned with proteins and/or peptides. There is no discussion of separating proteins on the resin taught by Hancock, nor is there a discussion of the use of the disclosed resin at a pH above 4.0.

If upon further consideration the examiner believes that an obviousness rejection should be made, we encourage the examiner to clearly articulate such a rejection paying particular attention to identifying why the combination of references relied upon would have placed appellants' claimed invention in the hands of a person of ordinary skill in the art at the time the invention was made.

IV. Enablement:

Appellants' claimed invention is directed to a resin-protein/peptide complex. As we understand it, this complex relies on the pI of the target protein/peptide. In addition, according to the claimed invention "about 50 percent or more of the target protein or peptide in an aqueous medium binds to

the resin when the aqueous medium has either a high or a low ionic strength." See e.g., claim 1. Assuming that the aqueous media is a whole cell extract, we would encourage the examiner to take a step back and determine whether the resins disclosed in appellants' specification would be capable of binding a single "target" protein/peptide, from such an aqueous media. It may be that a number of proteins, of which only one is the so-called target protein/peptide, in a cell extract may exhibit the same pI.

Accordingly, we encourage the examiner to take a step back, and review the claimed invention in light of the specification to determine whether a person of ordinary skill in the art would find it reasonable for a resin to bind a single "target" protein from any aqueous media, particularly an aqueous media that contains other proteins/peptides of similar size and pI.

VACATED and REMANDED

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|---|---|
| Joan Ellis<br>Administrative Patent Judge | ) |
| Toni R. Scheiner<br>Administrative Patent Judge | ) BOARD OF PATENT<br>APPEALS AND<br>INTERFERENCES |
| Donald E. Adams<br>Administrative Patent Judge | ) |

SHEPPARD, MULLIN, RICHTER & HAMPTON LLP
333 SOUTH HOPE STREET
48TH FLOOR
LOS ANGELES CA 90071-1448